UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,403	02/27/2004	Andrea Crisanti	GJE-39D1	5324

7590 01/06/2010

LILA A .HAILE, J.D.,PH.D
DLA Piper US LLP
4365 Excutive Drive, Suite 1100
San Diego, CA 92121-2133

EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
01/06/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,403	CRISANTI, ANDREA	
	Examiner	Art Unit	
	Karen Cochrane Carlson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *2,3 and 7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6 and 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/486,676.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group II, Claims 1, 4-6, and 13-16 as drawn to antennapedia homeodomain/regulatory protein fusion protein in the reply filed on October 14, 2009 is acknowledged.

The Examiner has withdrawn Claims 2, 3, 7-12 from further consideration because these claims are drawn to non-elected inventions.

Benefit of priority is to September 2, 1997.

The disclosure is objected to because of the following informalities:

The priority information at page 1 needs to be updated.

Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-6, and 13-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 refers to a functional variant of the homeodomain of antennapedia. This functional variant is not understood because the specification does not provide a definition for this term such that one skilled in the art could know the meets and bounds of this variant. For example, this term could include any transport protein, or a specific mutational variant of the homeodomain having transport activity.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Schutze-Redelmeier et al. (IDS; July 15, 1996; Introduction of Exogenous antigens into the MHC Class I processing and presentation pathway by Drosophila antennapedia homeodomain primes cytotoxic T cells in vivo. J. Immunol. 157: 650-655).

Schutze-Redelmeier et al. teach fusion proteins comprising the homeodomain of antennapedia and amino acids 170-179 of HLA-Cw3 CTL epitope (R2 and R4) or amino acids 147-156 of influenza nucleoprotein peptide (2.3.5) in Figure 1. The R2 and R4 fusion protein further comprised a C-terminal c-myc tag while the 2.3.5 fusion protein further comprised a C-terminal SIV tag. The fusion proteins were made recombinantly by transforming E. coli with expression vectors comprising nucleic acid encoding them. The fusion proteins R2 and R4 and the 2.3.5 were isolated on non-denaturing PAGE and western blotting using anti-human c-myc antibody or anti-tag SIV mAb, respectively (page 651, left., col, para 2). Cells were incubated with the fusion proteins (page 651, right col., para. 2) and therefore the fusion proteins were placed into a pharmaceutical composition. Mice were immunized with IFA emulsions comprising the R4 fusion protein (page 651, right col., para. 3), and therefore placed into a pharmaceutical composition.

Therefore, Schutze-Redelmeier et al. teach a conjugate comprising a first homeodomain of antennapedia and a second epitopic region of HLA-Cw3 CTL (R2 and R4) or influenza (2.3.5), wherein the conjugates are not denatured (**Claim 1**), wherein the conjugates are fusion proteins (**Claim 4**), wherein the conjugate was made recombinantly by transforming E. coli with expression vectors comprising nucleic acid encoding them. The fusion proteins R2 and R4 comprising the c-myc tag tail and the 2.3.5 comprising the SIV tag tail were isolated by affinity purification on non-denaturing PAGE and western blotting using anti-human c-myc antibody or anti-tag SIV mAb, respectively (**Claim 15, 16**). The R4 fusion protein was placed into IFA emulsions (**Claim 13**) and therefore in the form of a vaccine to immunize mice (**Claim 14**).

Claims 1, 4-6, 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Saffman et l. (1994; A differential response element for the homeotics at the antennapedia P1 promoter of Drosophila. Proc. Natl. Acad. Sci. 91: 7420-7424).

Saffman et al. teach fusion proteins comprising different regulatory elements of 3 different homeotic proteins, ultrabithorax (UBX), abdominal-A (ABD-A), and antennapedia (ANTP). Homeotic proteins are a family of related but distinct developmental regulators that specify the differences in the body segments of Drosophila (page 7420, left col., top). Saffman et al. teach fusion protein UAU in Fig. 3. The fusion protein UAU comprises the homeodomain of antennapedia and ultrabithorax homeoprotein N-terminal and C-tail. Fusion protein UAA comprises the homeodomain

and C-tail of antennapedia and the N-terminal of ultraithorax. In both of these fusion proteins, the ultrabithorox N-terminal region is at least 225 amino acids because the deletional mutant of ultrabithorax (*UU) has amino acids 37-225 deleted (page 7421, right col., line above 1st full para.), and the depiction of this deletional mutant and the UAU and UAA fusion protein in Fig. 3 shows the N-terminal region of ultrbithorax as comprising these amino acids plus additional amino acids N- and C-terminal to this deleted region. The fusion proteins were recombinantly produced via transformation of of S2 cells with expression vectors comprising nucleic acid encoding the fusion proteins. The fusion proteins were isolated via immunoblotting S2 extracts with UBX antibody (page 7421, right col., line 16-17). The "apparent molecular weight" was determined (page 7421, right col., line 17), indicating that the fusion proteins were not denatured.

Therefore, Saffman et al. teach a conjugate comprising a first region comprising the first homeodomain of antennapedia and a second ultrabithorax N-terminal region that is not naturally associated with the homeodomain of antennapedia and the fusion protein was not denatured (**Claim 1**), wherein the conjugate is in the form of a fusion protein (**Claim 4**), wherein the second ultrabithorax N-terminal region comprises at least 100 amino acids (**Claim 5),** and is a functional or regulatory protein (**Claim 6**). As noted above, the conjugates were produced recombinantly and isolated by UBX antibody affinity purification under non-denaturing conditions (**Claim 15**). Saffman et al. do not disclose where the UBX antibody binds within the isolated fusion. However, the UAU fusion protein comprises the UBX N- terminus and C-terminal tail, and the UAA

comprises the N-terminus tail. Therefore, the fusion protein comprise an amino acid tail that binds to an immobilised substrate (**Claim 16**).

Art of Record:

Perez et al. (1994; Rab3A and Rab3B carbosy-terminal peptides are both potent and specific inhibitors of prolactin release by rat cultured anterior pituitary cells. Mol. Endocrin. 8: 1278-1287) teach a recombinantly produced fusion protein comprising the homeodomain of antennapedia and the entire Rab3A protein (page 1279, right col., para. 4; Fig 3; page 1284, right col., para. 4.). However, this fusion protein was purified via SDS-PAGE (page 1285, left col, line 4), which SDS is a reducing/denaturing agent. Using this same purification method for fusion proteins comprising the homeodomain of antennapedia and smaller fragments of Rab3A, Perez et al. demonstrate that these fusion proteins could translocated across cell membranes while the fusion proteins with the full-length Rab3A could not.

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson whose telephone number is 571-272-0946. The examiner can normally be reached on 6:00 AM - 4:00 PM, Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen Cochrane Carlson/
Primary Examiner, Art Unit 1656